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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/568,637

03/22/2007

Johan Auwerx

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05/12/2009

NOVARTIS INSTITUTES FOR BIOMEDICAL RESEARCH, INC.

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CAMBRIDGE, MA 02139

EXAMINER

EWOLDT, GERALD R

ART UNIT

PAPER NUMBER

1644

MAIL DATE

DELIVERY MODE

05/12/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/568,637

Applicant(s)

AUWERX ET AL.

Examiner

G. R. Ewoldt, Ph.D.

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 February 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 1-10 and 18-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/CIS)
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☒ Other: Notice to Comply, Sequence
- Paper No(s)/Mail Date: _____

DETAILED ACTION

1. Applicant's election without traverse of Group I, Claims 15-17, is acknowledged.

Claims 1-10 and 18-21 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Claims 15-17 and linking claims 11-14 (as they read on the elected invention) are under examination.

2. The Declaration is objected to:

A) Uninitialed changes have been made to the residence and address of Inventor Thomas.

B) Uninitialed changes have been made to the residence and address of Inventor Sticker-Jantscheff.

C) There is no state listed in the residence and address of Inventor Kozma.

A new declaration is required.

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825. Specifically, no Sequence Listing or CRF has been submitted. Additionally, all sequences in the specification must be identified by SEQ ID NO:.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 11-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. There is insufficient evidence that the claimed method would be effective for the treating or preventing of insulin resistance or

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diabetes.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

A review of the art shows that Pende et al. (2000) investigated glucose homeostasis in S6K1 deficient mice almost a decade ago. The investigators found that S6K1 deficient mice were hypoinsulinanemic and glucose intolerant. They concluded, "... impaired S6K1 function may contribute with other genetic and environmental factors to the development of specific forms of diabetes mellitus." It would seem then that in light of these findings the impairment of S6K1 by the administration of an inhibitor of S6K1 would not likely provide an effective treatment for insulin resistance and/or diabetes. More recently, Fraenkel et al. (2008) actually administered an inhibitor of S6K1 (the mTOR inhibitor rapamycin, mTOR being the

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upstream effector of S6K1) and concluded, "Rapamycin induces fulminant diabetes by increasing insulin resistance and reducing β -cell function and mass. ... It is likely that treatments based on mTOR inhibition will cause exacerbation of diabetes." Clearly then, the most recent evidence *demonstrates* that the administration of an inhibitor of S6K1 would not provide an effective treatment for insulin resistance and/or diabetes. Contrast these findings with those of the specification wherein no inhibitors of S6K1 were actually administered in any insulin resistance of diabetes model. Instead, the Inventors merely showed that S6K1 deficient mice on a high fat diet were less insulin resistant than were wild type mice on a similar diet.

As set forth in *Rasmusson v. SmithKline Beecham Corp.*, 75 USPQ2d 1297, 1302 (CAFC 2005), enablement cannot be established unless one skilled in the art "would accept without question" an Applicant's statements regarding an invention, particularly in the absence of evidence regarding the effect of a claimed invention. Specifically:

"As we have explained, we have required a greater measure of proof, and for good reason. If mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to "inventions" consisting of little more than respectable guesses as to the likelihood of their success. When one of the guesses later proved true, the "inventor" would be rewarded the spoils instead of the party who demonstrated that the method actually worked. That scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis."

Thus, in view of the quantity of experimentation necessary, the lack of sufficient guidance in the specification, the lack of any working examples, i.e., the specification discloses no data demonstrating the treatment or prevention of insulin resistance or diabetes, even in animal models, and the demonstrated unpredictability of the art, it would take undue trials and errors to practice the claimed invention.

6. Claims 11-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Under *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession* of the invention, and that the invention, in that context, is whatever is now claimed.

There is insufficient written description to show that Applicant was in possession of the "S6 kinase 1 inhibitor" or an inhibitor "that preferentially reduces S6K1 activity compared to S6K2 [activity?]." of the claims. An adequate written description of the inhibitors of the claims would require either an adequate description of a common structure and a common function, or a disclosure of a representative number of inhibitor species. While some attempt has been made at disclosing a common function, i.e., inhibiting S6K1 kinase (though precisely what function is inhibited is not defined in independent Claim 11), there is no discussion of a common structure. Indeed, it is clear that no common structure exists given the disclosure of asserted inhibitory peptides (page 19) which would have no structure common to both the peptides and the antibody inhibitors. Accordingly, the specification must disclose a representative number of species describing the claimed genus of S6K1 inhibitors. S6K1 inhibitory antibodies are implied to exist in the prior art, though none are disclosed. S6K1 inhibitory peptides are asserted to exist but there is no demonstration of their *in vivo* efficacy (peptides are generally extremely short-lived *in vivo*). There is no disclosure at all of inhibitors that preferentially reduces S6K1 activity compared to S6K2. Accordingly, given the minimal showings of the instant specification, one of skill in the art would conclude that the specification fails to disclose either a representative number of species, or common functional and structural characteristics, adequate to describe the claimed genus of inhibitors of S6K1 required for use in the claimed method. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

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7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

e) the invention was described in--

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

8. Claims 11 and 13 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by U.S. Patent No. 5,321,009.

The '009 patent teaches a method of treating diabetes, which would encompass insulin resistance, comprising the administration of rapamycin. As set forth above, rapamycin is an inhibitor of mTOR (an upstream effector of S6K1) and thus, can be considered to be an inhibitor of S6K1. Note that the *in vivo* administration of rapamycin would comprise its contacting of an adipocyte, myocyte, and hepatocyte.

The reference teaching anticipates the claimed invention.

9. Claims 11 and 13 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by U.S. Patent Application Publication No. 2007/0053910.

The '910 publication teaches a method of treating or preventing a weight disorder that would inherently comprise a method of treating diabetes (encompassing insulin resistance), comprising the administration of an inhibitor of S6K1 (Claim 12 of the '910 publication). The method further encompasses the administration of inhibitors reciting the limitations of Claims 12 and 14-17 of the instant application (Claims 13-16 of the '910 publication).

The reference teaching anticipates the claimed invention.

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 11-17 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-16 of copending Application No. 10/531,515. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims recite the same steps of the administration of various S6K1 inhibitors that would inherently treat insulin resistance and diabetes.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on (571) 272-0878.

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14. **Please Note:** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

/G.R. Ewoldt/
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